



PHA2005.1 (3167/8Z/US)
PATENT

IN THE CLAIMS:

Claims 1 - 140. (Cancelled)

Claim 141. (Currently amended) A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to said mammal a therapeutically-effective amount of a combination of celecoxib and an integrin antagonist selected from the group of compounds consisting of:

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[[5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[[1,6-dihydro-6-oxo-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-amino-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-[(hydroxyamino)carbonyl]-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy)-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-[(4, 5-dihydro-1H-imidazol-2-yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3, 5-dichloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-b-alanine; and

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claims 142 - 143. (Cancelled)

Claim 144. (Currently amended) A combination comprising celecoxib and an integrin antagonist selected from the group of compounds consisting of:

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[[5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[[1,6-dihydro-6-oxo-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-amino-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-[(hydroxyamino)carbonyl]-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-[(4, 5-dihydro-1H-imidazol-2-yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3, 5-dichloro-2-hydroxyphenyl)-b-alanine;

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-b-alanine; and

(3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 145. (New) The method of claim 141 wherein the neoplasia disorder is selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma, carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma, hemangioblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, intraepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, lentigo maligna melanomas, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma, nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, pituitary tumors, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinomas, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor.

Claim 146. (New) The method of claim 141 wherein the neoplasia disorder is lung cancer.

Claim 147. (New) The method of claim 141 wherein the neoplasia disorder is colorectal cancer.

Claim 148. (New) The method of claim 141 wherein the neoplasia disorder is breast cancer.

Claim 149. (New) The method of claim 141 wherein the neoplasia disorder is prostate cancer.

Claim 150. (New) The method of claim 141 wherein the neoplasia disorder is bladder cancer.

Claim 151. (New) The method of claim 141 wherein the neoplasia disorder is ovary cancer.

Claim 152. (New) The method of claim 141 wherein the neoplasia disorder is cervical cancer.

Claim 153. (New) The method of claim 141 wherein the neoplasia disorder is gastrointestinal cancer.

Claim 154. (New) The method of claim 141 wherein the neoplasia disorder is head and neck cancer.

Claim 155. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 156. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[[5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 157. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[[1,6-dihydro-6-oxo-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 158. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-amino-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 159. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-[(hydroxyamino)carbonyl]-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy)-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 160. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-[(4, 5-dihydro-1H-imidazol-2-yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 161. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 162. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3, 5-dichloro-2-hydroxyphenyl)-b-alanine.

Claim 163. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-b-alanine.

Claim 164. (New) The method of claim 141 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 165. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 166. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[[5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 167. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[[1,6-dihydro-6-oxo-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 168. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-amino-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 169. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-[(hydroxyamino)carbonyl]-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy)-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 170. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-[(4, 5-dihydro-1H-imidazol-2-yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 171. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.

Claim 172. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3, 5-dichloro-2-hydroxyphenyl)-b-alanine.

Claim 173. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-b-alanine.

Claim 174. (New) The combination of claim 144 wherein the integrin antagonist is (3R)-N-[3-hydroxy-5-[(1, 4, 5, 6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine.